Full Title: Does increasing applied load lead to contact changes indicative of knee osteoarthritis? A subject-specific FEA study.

Short Title: A subject-specific FEA study into the link between obesity and knee OA

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Abstract

This study investigated whether increased loading (representing obesity) in the extended knee and flexed knee led to increased stresses in areas of typical medial and lateral osteoarthritis cartilage lesions, respectively. We created two paired sets of subject-specific finite element models; both sets included models of extended knees and of flexed knees. The first set represented normal loading; the second set represented increased loading. All other variables were held constant. The von Mises stresses and contact areas calculated on the tibial cartilage surfaces of the paired models were then compared.

In the extended knee models, applying a larger load led to increased stress in the anterior and central regions of the medial tibial cartilage. These are the typical locations of medial osteoarthritis cartilage lesions. Therefore, the results support that increased loading in the extended knee may result in medial osteoarthritis.

In the flexed knee models, applying a larger load increased stress in the anterior and central regions of the lateral tibial cartilage. Lateral osteoarthritis cartilage lesions typically occur centrally and posteriorly. Therefore, these results do not support our hypothesis. Shear stress was increased in areas of typical lateral lesions, however, and should be investigated in future studies.

Introduction

Osteoarthritis (OA) is common in the hand, spine, hip, and knee. Lower limb joints (hip and knee) are most affected by increased load/obesity, with a higher prevalence of OA in the knee than in the hip [1]. This study focused on the knee. Two common forms of unicompartmental knee OA are medial OA and lateral OA. Each form has distinct, repeatable cartilage lesion locations as well as corresponding flexion angles in which the tibial and the femoral cartilage lesions contact. Medial OA lesions initiate anteriorly and centrally [2-5]; the tibial and the femoral lesions contact near knee extension (10.9° ± 3.5°, [2]). Lateral OA lesions initiate centrally/posteriorly [2, 4]; the tibiofemoral lesions contact in mid-range flexion (40.5° ± 2.9°, [2]). We, therefore, propose that the initiation of medial OA and lateral OA are attributed to loading during knee extension and knee flexion, respectively. Extra body weight associated with obesity may increase stress within the joint, damaging the cartilage and resulting in OA.

Large-scale population-based studies and systematic reviews have shown that obesity is a risk factor for OA [6-8]. Proposed mechanisms of medial OA and lateral OA initiation can be investigated using finite element (FE) models. FE models allow the calculation of variables, such as stress and strain, which could not ethically be measured *in vivo* in healthy subjects (obtaining these variables would require inserting pressure film during surgery). Generic FE models combine generic or idealized geometries and loads. These models are faster to generate, but the smoother, idealized geometries result in overestimated contact areas and underestimated contact stresses [9]. Conversely, subject- or patient-specific FE models combine geometry and loads derived from a single individual. These models require more time to create, but are particularly useful when subject-specific variables are desired.

This study used subject-specific FE models to investigate the effect that increased load had on the stress patterns in extended and flexed knees. Locations of increased stress were then compared to typical locations of medial OA and lateral OA cartilage lesions. This study is novel because most studies only include models of the extended knees, perhaps because of the difficulty of determining the individual bone positions in the flexed knee. It is vital to also investigate stresses within the flexed knee, however, particularly when loading during flexion is hypothesized to lead to lateral OA.

Methods

Data Collection and Processing

Motion analysis and MRI data were collected from 3 healthy subjects: 2 female, 1 male; aged 23-30 years; BMI 21.0–23.7 (ethical approval: 07/Q1604/27, Oxfordshire Research Ethics

Committee). Informed consent was given and absence of MRI contra-indications was verified prior to data collection.

Motion analysis began by recording each subject's height, weight, lower limb lengths, distances between anterior-superior iliac spine prominences, and widths of the ankles and knees. Then, retro-reflective markers were placed on bony landmarks (Figure 1) according to an adapted Helen Hayes marker set [10] (posterior superior iliac spine, anterior superior iliac spine, greater trochanter, thigh (wand), tibia (wand), shin, ankle, medial malleolus, heel, toe, distal first metatarsal, and distal fifth metatarsal of both the right and left limbs and sacrum). Additional registration markers (shown as unfilled circles) were placed around the knee (medial femoral epicondyle, lateral femoral epicondyle, mid thigh superior to patella, superior lateral patella, tibial tuberosity, medial tibial condyle, and fibular head); these markers were later used to register the motion analysis and MRI data. After marker placement, subjects completed cycles of level walking and sit-to-stand within the capture volume of a 12 camera video-based motion analysis system. Marker trajectory data (Vicon 612, Vicon Motion Systems Ltd., Oxford, UK) and ground reaction force data (OR6 platform, Advance Mechanical Technology Inc., Watertown, MA, USA) were collected during these activities.

Marker and force plate data were used as input to a lower limb musculoskeletal model (AnyBody Technology Version 3.0, AnyBody Technology A/S, Aalborg, Denmark). This model included seven segments (one pelvis and a thigh, shank, and foot segment on each side of the body), totaling to eighteen kinematic degrees of freedom. The pelvis, hip, knee, and ankle had six, three (internal-external rotation, flexion-extension, adduction-abduction), one (flexion-extension), and two (plantar flexion-dorsi flexion, inversion-eversion) degrees of freedom, respectively. This model includes 42 individual muscles (9 of which represented the gluteal muscle group), each modelled as a Hill-type muscle, on each lower limb. First, models were tailored to each subject's specific anthropometrics. Subject height was used to scale limb lengths and muscle insertion/origin locations; subject weight was used to scale limb weights. Then, the subject- and task-specific motion recorded during motion analysis was re-created within the musculoskeletal model. The models then used a min-max optimization criterion [11] to estimate muscle and joint reaction loads during the recorded motions.

Immediately following motion analysis, MRI data was collected. The black markers shown in Figure 1 were removed. The unfilled markers shown in Figure 1 were replaced by fluid-filled MRI registration markers (MM3002 Multi-Modality Fiducial Markers, IZI Medical, Owings Mills, MD, USA). Separate non-weight-bearing MRI scans (3T T1-weighted multislice, MobiView Philips Medical Systems/Achieva, Best, The Netherlands) were taken of the right and left knees in near extension (~5°) and mid-range (~50°) flexion. Foam

wedges maintained the flexion angles during scanning. MRI data was segmented (Mimics 13.0, Materalise, Leuven, Belgium) according to voxel greyscale intensity values to obtain the 3D surfaces of the tibia, femur, tibial cartilage, femoral cartilage, and menisci. The seven registration marker locations were also identified. Generated structure surfaces were checked for integrity and discontinuities (Geomagic Studio 11, Geomagic, Inc., Research Triangle Park, NC, USA), and the resulting structures were assembled to create the knee model geometry (SolidWorks 2010, Dassault Systèmes SolidWorks Corp., Concord, MA, USA).

The MRI data and motion analysis data were originally collected in different coordinate systems. The two data sets were matched/registered (least-squares error minimization, [12]) using the seven registration markers included during both types of data collection. The total residuals for all seven registration markers were 12.1 mm ± 4.3 mm. The calculated loads (derived from the motion analysis data) were then transformed into the MRI coordinate system (Matlab R2007a, MathWorks, Natick, MA, USA).

FE Model Creation

Subject-specific geometries and loads were then combined to create the FE models (Abaqus 6.11, Dassault Systèmes, Providence, RI, USA). This FE model creation method was previously validated in a porcine validation study [13]. In the validation study, pressure films (K-Scan System Model 4201, Tekscan, Inc., South Boston, MA, USA) were inserted beneath the menisci of two porcine specimens. The specimens were then loaded with known loads (Zwick/Roell Z005, Zwick Testing Machines Ltd., Leominster, UK) while the pressure film recorded the pressures experienced on the tibial cartilage surfaces. The porcine specimens were then imaged using a 3T MRI scanner (T1-weighted multislice, MobiView Philips Medical Systems/Achieva, Best, The Netherlands). The MRI and load data were combined to create FE models. The pressures measured experimentally by the pressure film and calculated by the FE models were then compared. The two sets of pressures differed by less than 25%, a common threshold used for validation studies comparing pressure film and FE results [14].

In the current study, the validated model creation method was used to create two sets of models: “Physiological” models represented normal loading; “Overload” models represented increased loading. Paired Physiological and Overload models, with identical geometries but different applied loads, were created and compared (example in Figure 2). All other model parameters (material properties, boundary constraints, contact constraints) were identical for all models in this study.

The Physiological models were created first. These subject-specific models represented either level walking or sit-to-stand. Level walking models included extended knee geometry with loads calculated for heel strike during level walking. Sit-to-stand models included flexed knee geometry with loads calculated for the instant at which the knee flexion angle matched the angle recorded in the flexed knee MRI scan.

All material properties were assigned according to literature values (Table 1). Bone is much stiffer than cartilage and menisci. Bone was, therefore, modelled as a rigid material [15] to speed up model solution. Cartilage and menisci are both viscoelastic materials. The elapsed loading times during walking and sit-to-stand were significantly shorter than these tissues' viscoelastic time constants (~1500 seconds, [15]), however. Fluid would not have moved within these tissues during the short elapsed loading times. Therefore, cartilage and menisci were modelled as linear elastic isotropic and linear elastic transversely isotropic materials, respectively [16-17].

A unique subject- and task-specific 3D load was applied to each Physiological model. Loads were applied to the femur's center of mass while the tibia was fully constrained. Initially, the femur was allowed free translation and rotation, but these models had excessive femoral motion. To constrain this motion, an axial-translation-only boundary constraint was applied to the femur. This constraint was deemed valid, with the assumption that that the majority of the femur's motion in the instant represented by the FE models would be in the axial direction. As a consequence of this assumption, only the axial components of the 3D loads (Table 2) affected the models (non-axial loads were balanced by the femoral boundary constraints). No boundary constraints were applied to the cartilage or menisci.

Bone-cartilage interfaces were tied to represent the physiological calcified cartilage region. Cartilage-cartilage and cartilage-menisci interfaces were modelled using low-frictional contact ($\mu = 0.02$, [18]). This represented the physiological near frictionless conditions within the normal knee. Cartilage-cartilage and cartilage-menisci surfaces were not allowed to separate after coming into contact during model solution. This contact constraint also helped prevent excessive motion within the models. The constraint was considered valid since applying a load to the knee causes contact, rather than separation, between these soft tissues.

The models were meshed with Abaqus C3D4 tetrahedral elements. Element sizes were assigned based on mesh convergence test results [13]. Separate mesh convergence tests were conducted for the extended knees and flexed knees because it was not known (before the study began) whether the contact characteristics (contact area, stress values) would vary according to knee orientation angle. Femoral cartilage, tibial cartilage, and menisci elements,

respectively, had side lengths of 1.65 mm, 0.51 mm, and 0.78 mm in the extended knee models and 0.98 mm, 0.57 mm, and 0.38 mm in the flexed knee models. Models were solved using quasi-static double-precision explicit solution algorithms.

Next, the Overload models were created and solved. These models were identical to the Physiological models, with the exception of the applied loads. Instead of applying unique, subject-specific loads, a standardized 2000 N axial load was applied to each Overload model. This load corresponded to approximately three times body weight for each subject. Since each Physiological model had a unique load applied, the magnitude of load increase for each Physiological-Overload model pairing varied. The magnitude of load increase was significant in all pairings; Overload model loads were at least 3.5 times larger than the applied Physiological model loads.

Analysis of Model Outputs

To identify how specific areas of the tibial cartilage were affected by increased load, results were calculated for each of 12 locations on the tibial cartilage surface (Figure 3): the anterior (A), central (C), and posterior (P) areas of the inner (I) and outer (O) sections of the medial (M) and lateral (L) compartments. The average von Mises stress magnitude (VMS), cartilage-cartilage contact area, and cartilage-meniscus contact area were determined for each section. Contact area was reported as a percentage of the total cartilage surface in the individual section.

Results were analyzed in three ways. First, results of models within the same load set (i.e., all Physiological models) were compared to each other. The medial and lateral compartment locations with the highest VMS were identified. This analysis answered the questions "Where is VMS highest in knees with normal loads? Where is VMS highest in knees with increased loads?" Similarly, cartilage-cartilage and cartilage-meniscus contact area were calculated for each location, answering the question "Where does cartilage-cartilage and cartilage-meniscus contact typically occur in knees with normal and with increased loads?"

Second, paired Physiological and Overload results (i.e., Physiological and Overload models for Subject 1 R) were compared. For each Physiological – Overload pairing, the tibial cartilage locations with the highest VMS were compared. Then the percent differences in VMS for paired locations were calculated.

$$Diff = \frac{VMS\ in\ Overload\ model\ location - VMS\ in\ Physiological\ model\ location}{VMS\ in\ \text{Physiological}\ model\ location} * 100\%$$

Since each Physiological model had a different subject-specific load applied, percent differences were normalized according to the magnitude of applied load increase.

$$Normalized\ Diff = \frac{Diff}{Overload\ model\ load - Physiological\ \text{model}\ load},$$

where Overload model load = 2000 N in all cases.

This analysis answered the question "How does increased load affect VMS in individual knees?" Paired cartilage-cartilage and cartilage-meniscus contact area were also compared, with normalized percent differences calculated. This part of the analysis answered the question "How does increased load affect contact areas in individual knees?"

Third, the normalized percent differences of all of the models within a load condition were averaged (i.e., all the Physiological models). Comparing the averages in each location gave insight into where the highest VMS and largest contact area occurred. Considering the standard deviations gave insight into the variation of these variables between knees. This analysis answered the question "How does increased load generally affect VMS and contact areas in the knee?"

This study hypothesized that increased load would affect extended knees and flexed knees differently. Therefore, comparison results are reported separately for the extended knee and flexed knee models. The trends in VMS and contact area results were then used to propose potential mechanisms of medial OA and lateral OA initiation.

Results

Results were calculated for both right and left knees. Figures of left knee results have been reflected to allow for easier comparison of left and right knee results. The medial compartment is on the left side of all figures.

Models required 9 hours to 150 hours and 627.9 MB to 3.1 GB of total memory to solve on an Intel®Core2 Duo processor workstation running at 3.2 GHz with 3.25 GB of RAM.

Extended knees

The location on the medial tibial cartilage with the highest VMS varied between models. This was true both in the normal and increased load models. Lateral compartment VMS was highest in the anterior-central and inner locations for both applied load sets. Cartilage-cartilage contact occurred anteriorly-centrally, with little posterior contact, for the medial and

lateral compartments for both sets of loadings. Conversely, tibial cartilage-meniscus contact occurred predominantly posteriorly and in outer locations in both sets of loadings.

In the paired low and high load models, the highest stresses occurred in the same location in 10 of the 12 compartment pairings. For example, the highest medial and lateral VMS for Subject 1 R occurred in the central-outer and anterior-inner locations, respectively, for both Physiological and Overload models (Figure 4). VMS did not uniformly increase in all locations. Again, using Subject 1 R as an example, VMS increased in all locations, with larger VMS increases anteriorly, particularly in the medial compartment.

Typically, medial compartment VMS increased noticeably in the anterior-central locations; lateral compartment VMS increased frequently in the central-inner location (Figure 5). Averaged normalized percent differences (Figure 6) confirmed these trends. The largest VMS increases occurred in the medial anterior-inner (0.33 ± 0.20 %/N) and lateral central-inner (0.33 ± 0.12 %/N) locations. Large variability in VMS showed that the models had subject-specific model responses to the increased load.

Both paired and averaged results showed that medial and lateral cartilage-cartilage contact area increased anteriorly-centrally, with limited effect posteriorly, as applied load increased (Figure 7). Contact increased in both inner and outer sections of the medial compartment; lateral compartment contact increased in inner sections. Conversely, increased load had limited effect on anterior cartilage-meniscus contact area, with decreased anterior contact in some cases. Posterior cartilage-meniscus contact area increased with increased load.

Flexed knees

For both load conditions, the highest medial VMS occurred anteriorly-centrally and in the outer locations. Lateral VMS was highest anteriorly, as well as being high in the outer locations in the Overload models. In Physiological models, cartilage-cartilage contact area was greatest in the central-inner location, with no posterior contact. Cartilage-meniscus contact occurred in the outer locations, as well as posteriorly in the medial compartment and anteriorly in the lateral compartment. In Overload models, cartilage-cartilage contact again occurred in the central-inner location, but with posterior contact. Laterally, contact occurred in the anterior-central and inner locations, with no posterior contact. Cartilage-meniscus contact occurred in the posterior and anterior-outer locations in both the medial and lateral compartments.

In the paired models, the largest medial VMS increases occurred centrally (5 of 6 paired models), with either anterior or posterior increases each in 3 of 6 paired models (Figure 8). Laterally, there were no anterior-central-posterior trends for increased stress, but a tendency for increased stress in the inner locations.

On average, VMS increased in all areas of the medial compartment, except for the posterior-inner location (Figure 9). The largest VMS increases occurred centrally, particularly in the outer location (0.51 ± 0.43 %/N). Laterally, the largest VMS increases occurred in the inner anterior-central locations (0.51 ± 0.51 %/N and 0.52 ± 0.46 %/N, respectively). Large variability in VMS (sometimes as large as the average VMS result itself) again reflected the subject-specific model responses to increased load.

Both paired and averaged cartilage-cartilage contact area increased throughout the medial compartment, particularly in the central and inner anterior locations, as applied load increased (Figure 10). Laterally, contact increased in the inner anterior-central locations, with almost no change posteriorly.

The effect of increased load on cartilage-meniscus contact varied widely between models. In many paired models, contact area increased, particularly in the lateral compartment. In some pairings, however, contact area decreased, particularly in medial central and posterior locations. These subject-specific results led to large variations in averaged results (seen in error bar lengths, Figure 10). On average, contact increased anteriorly in the medial compartment and in all locations in the lateral compartment, particularly in anterior and posterior locations. Contact area decreased in the medial central-posterior inner locations.

Discussion

The effects of applying an increased load varied between models. These variations were not surprising. Each model represented the specific geometry of an individual knee. Geometry directly affects where contact occurs, consequently affecting calculated stresses. Calculated stresses are also affected by the load applied. Even when a standardized load was applied (Overload models), different geometries resulted in different stress patterns. This finding supports the importance of using subject-specific geometry.

There were some repeatable trends within the models. VMS was higher and cartilage-cartilage contact area generally increased when larger loads were applied. The effects of increased load on cartilage-meniscus contact area varied; contact area increased in some models and decreased in other models. The VMS and contact area trends were related.

Larger applied loads brought more of the cartilage and menisci surfaces into contact. The femoral cartilage and tibial cartilage were pushed together, increasing cartilage-cartilage contact, particularly in inner locations. In some models, the menisci accommodated this increased cartilage-cartilage contact by moving peripherally (predominantly anteriorly and posteriorly and to a lesser extent medial-laterally). Similar meniscal motion accommodation has also been described elsewhere [19]. The edges of the menisci then extended beyond the edges of the tibial cartilage, decreasing cartilage-meniscus contact area.

In the extended knee models, stress predominantly increased anteriorly and centrally. These locations of increased medial compartment VMS (anterior and central) corresponded well with the established locations of medial OA cartilage lesions [2-5]. Therefore, this study supports the hypothesis that increased load in the extended knee leads to increased stress and potentially to cartilage damage associated with OA. Lateral compartment VMS also increased anteriorly and centrally, especially in the inner locations. These locations do not match the typical lateral OA cartilage lesion locations [2, 4]. Lateral OA was hypothesized to be linked to loading during mid-range flexion, however, so this mismatch between locations of increased VMS and typical cartilage lesion was not unexpected.

In the flexed knee models, VMS and contact area were hypothesized to increase in the central and posterior areas of the lateral compartment. Surprisingly, posterior VMS only noticeably increased in 1 of the 6 paired models. Stresses were low in the posterior sections because the posterior sections were rarely in contact. Instead, VMS noticeably increased centrally in 3 of the 6 model pairs. This study therefore gives limited support to the hypothesis that increased load in the flexed knee leads to increased stress in central and posterior locations. Conversely, this study suggests that loading during flexion increases stress in the anterior and central locations of the lateral tibial cartilage.

It could have been possible that this mismatch between locations of increased VMS and typical lateral OA cartilage lesions was due to the model setup. Ligaments were not included in the models, despite playing an important role in joint stability. To test whether including ligaments would change the results, the ACL, PCL, LCL, MCL, anterior inter-meniscal ligament, and posterior capsule were added to 2 of the 6 model pairings (Subject 2, L and R). Ligament insertion/origin locations were identified in the MRI scans and so were subject-specific. Ligaments were modelled as uniaxial springs, with nonlinear force-displacement material properties taken from the literature [20-22]. Including the ligaments meant that the femur could be allowed free motion (with only the flexion angle constrained), and that the soft tissue surfaces could be allowed to separate during model solution. The results of these re-run models were then compared to the results of the no-ligament models.

These re-run ligament models again had contact and increased stress almost exclusively in the anterior and central locations. This was because the 3D applied loads now included an anterior force, shifting the femur forward onto anterior areas of the tibia. Anterior applied forces were calculated for 11 of the 12 models (the 12th model had a posterior force of 10 N). Therefore, it is expected that neither the re-run ligament models nor the previous no-ligament models would have had predominantly posterior contact as assumed in our hypothesis.

It might have been possible that the method of load increase may have affected the results. In the results presented, all Overload model loads were increased to a standardized 2000 N. The loads could have also been increased by a certain percentage, however, for example doubling each Physiological model load. To investigate the effect of setting the Overload model loads to a standardized or relative increased load, all flexed knee models were solved with both the standardized 2000 N load and with a relative load of twice the Physiological model load. The patterns of where the highest stresses occurred were the same regardless of which load was applied. Therefore, the method of increasing the loads did not affect these results. For ease of presenting results, only the standardized load results are including in this manuscript.

Finally, it is also possible that a variable other than VMS leads to the cartilage lesions seen in lateral OA. For example, shear stresses were elevated in the posterior locations of the re-run Overload ligament models. The mesh convergence test conducted for this study only tested for convergence of VMS and contact pressure, however, making it inappropriate to extract results later for other variables from the models. Further studies could be conducted to investigate how increased loading affects additional contact variables, such as shear stress.

Overall, this study highlights the importance of maintaining a healthy body weight and limiting the body's exposure to avoidable high loads. That obesity leads to increased stress within the body's tissues is not surprising. The main contribution of this study was establishing a link between increased applied load in the *extended* knee in particular and increased cartilage stresses in areas where medial OA is known to occur *specifically*.

Limitations and Assumptions

Ligaments contribute to *in vivo* knee stability by restricting excessive motion. They are also an integral part of the four-bar linkage system used to describe dynamic motion within the knee [23]. Ligaments were not included in the FE models, however, due to their probable addition in model complexity and solution time (the models already required 9 – 150 hours for solution). Instead, excessive motion was limited by constraining the femur to axial-only translation. This boundary constraint was used under the condition that the FE models represented quasi-static conditions, and under the assumption that model geometry would not

noticeably rotate or translate in the anterior-posterior or medial-lateral planes during model solution. This assumption was considered valid since model geometry had been pre-positioned into the desired flexion/extension angle, with a maximum of 0.5 mm separating the various structures. It is also important to note that these boundary constraints were consistent between Physiological and Overload model pairs, so comparing trends of changes within pairings was valid.

A limitation of this study was using literature-derived rather than subject-specific material properties for cartilage and menisci. Subject-specific properties cannot currently be determined non-invasively. Therefore, this study used material properties commonly cited in the literature for other FE models of the normal knee. In the future, FE models would ideally incorporate not only subject-specific geometry and loads but also material properties. Specific material properties are of even greater importance when modelling diseased, rather than healthy, joints. The models in this study were all of normal knees, however, so using literature-derived values was deemed permissible.

A 2000 N load was applied to Overload models, representing at least a 3.5 time increase in load at heel strike and the instant of sit-to-stand. The load increase was, therefore, appropriate to answer our specific research questions. It should be noted, however, that 2000 N corresponded to approximately three times body weight for these subjects. Instrumented knee implants show that the peak tibiofemoral load experienced during activities such as climbing stairs is approximately three times body weight [24]. Loads experienced during more strenuous activities such as running and jumping would be larger. Therefore, it should be emphasized that this study sought to investigate the effects of increasing the normal load experienced at specific instants and flexion/extension angles, rather than applying loads which would never be experienced by the normal knee.

Conclusions

This study compared paired sets of models, identical in all parameters except for applied load. In the first set, subject-specific normal loads were applied; in the second set, a standardized 2000 N load (representing an increase of at least 3.5 times in load) was applied. Each set contained models of the extended knee as well as models of the flexed knee. Models with different tibiofemoral flexion angles were created to test the hypothesis that increased load in extended and flexed knees increases stress in typical areas of medial OA and lateral OA cartilage lesions, respectively. To test this hypothesis, VMS and contact area for each paired set of models were recorded and compared.

In the extended knee models, VMS increased anteriorly and centrally in the medial compartment. These areas of high stress match intraoperatively-measured locations of medial OA cartilage lesions. Therefore, this study supports the hypothesis that increased load in the extended knee results in increased stress, which could then potentially result in cartilage damage and medial OA.

In the flexed knee models, VMS increased in the inner anterior and central locations in the lateral compartment. These locations do not match intraoperative areas of lateral OA cartilage lesions. It was thought that the model set-up may have caused this mismatch, so some models were solved again with ligaments included. These ligament-included models also did not have contact in areas of typical lateral OA cartilage lesions. Shear stress was increased in typical lesion locations, however. Future studies could investigate whether increased load increases shear stress in the flexed knee – perhaps this contact variable may explain why cartilage damage occurs and leads to lateral OA.

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Table 1: Material properties used in the FE models.

	Material Property	Reference
Bone	Rigid	[14]
Cartilage	E = 12 MPa, ν = 0.45	[15]
Menisci (axial, radial)	E = 20 MPa, ν = 0.2	[16]
(circumferential)	E = 120 MPa, ν = 0.3	[16]

Table 2: Loads (N) applied to Physiological models.

Subject	**Left knee**	**Right knee**
Extended Knees		
Subject 1	206	532
Subject 2	325	396
Subject 3	285	424
Flexed Knees		
Subject 1	73	126
Subject 2	270	196
Subject 3	518	296